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DATE: Monday, February 07, 2005

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|--------------------------|---------------------------|--|----------------------------|
|                          |                           | <i>DB=USPT; PLUR=YES; OP=AND</i>   |                            |
| <input type="checkbox"/> | L1                        | 5919665.pn.  | 1                          |
| <input type="checkbox"/> | L2                        | botulinum.clm. same toxin.clm.   | 121                        |
| <input type="checkbox"/> | L3                        | L2 and (truncat\$ or domain or domains or region or regions or portion or portions or chain or chains or fragment or fragments).clm. | 47                         |

END OF SEARCH HISTORY

## Search Results - Record(s) 1 through 9 of 9 returned.

- 
- ☐ 1. 20040253673. 05 Dec 03. 16 Dec 04. Recombinant botulinum toxins with a soluble C-terminal portion. Williams, James A.. 435/69.1; 435/252.33 435/254.2 435/320.1 435/348 530/350 536/23.7 C07K014/33 C07H021/04 C12N001/21.
- 
- ☐ 2. 20040235118. 04 Dec 03. 25 Nov 04. Portions of soluble recombinant botulinum toxins. Williams, James A.. 435/69.7; C12P021/04.
- 
- ☐ 3. 20040219637. 05 Dec 03. 04 Nov 04. Soluble recombinant botulinum toxins having a C-terminal portion of a heavy chain, a N-terminal portion of a heavy chain and a light chain. Williams, James A.. 435/69.3; 435/252.33 435/254.2 435/320.1 435/348 C12P021/02 C12N001/18 C12N005/06.
- 
- ☐ 4. 20040142455. 05 Dec 03. 22 Jul 04. Recombinant botulinum toxins having a soluble C-terminal portion of a heavy chain, an N-terminal portion of a heavy chain and a light chain. Williams, James A.. 435/252.33; 435/254.2 435/320.1 435/348 435/69.3 530/350 536/23.7 C12P021/02 C12N001/21 C12N001/18 C12N005/06.
- 
- ☐ 5. 20040115215. 05 Dec 03. 17 Jun 04. Recombinant botulinum toxins with a soluble C-terminal portion, an N-terminal portion and a light chain. Williams, James A.. 424/184.1; A61K039/395 A61K039/00 A61K039/38.
- 
- ☐ 6. 20030219457. 15 Oct 02. 27 Nov 03. Soluble recombinant botulinum toxins. Williams, James A.. 424/199.1; 424/186.1 424/234.1 435/6 C12Q001/68 A61K039/12 A61K039/02.
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- ☐ 7. 20030215468. 30 Jan 03. 20 Nov 03. Soluble recombinant botulinum toxin proteins. Williams, James A., et al. 424/239.1; 435/252.3 435/70.21 530/388.4 A61K039/08 C12P021/04 C12N001/21 C07K016/12.
- 
- ☐ 8. 20030118547. 14 Nov 02. 26 Jun 03. Composition for intestinal delivery. Vandenberg, Grant William. 424/85.4; 424/130.1 424/85.2 424/93.2 514/169 514/2 514/54 514/560 A61K048/00 A61K038/21 A61K031/715 A61K038/24 A61K038/20 A61K031/573 A61K031/20 A61K031/56 A61K039/395.
- 
- ☐ 9. 20030108597. 13 Aug 02. 12 Jun 03. Application of lipid vehicles and use for drug delivery. Chancellor, Michael B., et al. 424/450; 424/143.1 424/239.1 424/760 514/44 514/625 A61K048/00 A61K039/395 A61K009/127 A61K035/78 A61K031/16 A61K039/08.
-

DERWENT-ACC-NO: 1998-230234

DERWENT-WEEK: 200482

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TITLE: Host cell containing recombinant expression vector encoding Clostridium botulinum type B or E toxin - useful to treat humans and other animals at risk of intoxication with clostridial toxin

INVENTOR: THALLEY, B S; WILLIAMS, J A

PATENT-ASSIGNEE: OPHIDIAN PHARM INC (OPHIN), ALLERGAN BOTOX LTD (ALLR),  
ALLERGAN INC (ALLR), ALLERGAN SALES INC (ALLR)

PRIORITY-DATA: 1996US-0704159 (August 28, 1996), 1995US-0405496 (March 16, 1995), 2003US-0354774 (January 30, 2003), 2002US-0271012 (October 15, 2002), 2003US-0729122 (December 5, 2003), 2003US-0729039 (December 5, 2003), 2003US-0729527 (December 5, 2003), 2003US-0727898 (December 4, 2003), 2003US-0728696 (December 5, 2003)

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## PATENT-FAMILY:

| PUB-NO  | PUB-DATE          | LANGUAGE | PAGES | MAIN-IPC    |
|---|-------------------|----------|-------|-------------|
| <input type="checkbox"/> <u>US 20040253673 A1</u> | December 16, 2004 |          | 000   | C07K014/33  |
| <input type="checkbox"/> <u>WO 9808540 A1</u>     | March 5, 1998     | E        | 427   | A61K039/00  |
| <input type="checkbox"/> <u>AU 9742450 A</u>      | March 19, 1998    |          | 000   |             |
| <input type="checkbox"/> <u>EP 1105153 A1</u>     | June 13, 2001     | E        | 000   | A61K039/00  |
| <input type="checkbox"/> <u>US 20030215468 A1</u> | November 20, 2003 |          | 000   | A61K039/08  |
| <input type="checkbox"/> <u>US 20030219457 A1</u> | November 27, 2003 |          | 000   | C12Q001/68  |
| <input type="checkbox"/> <u>US 20040115215 A1</u> | June 17, 2004     |          | 000   | A61K039/395 |
| <input type="checkbox"/> <u>US 20040142455 A1</u> | July 22, 2004     |          | 000   | C12P021/02  |
| <input type="checkbox"/> <u>US 20040219637 A1</u> | November 4, 2004  |          | 000   | C12P021/02  |
| <input type="checkbox"/> <u>US 20040235118 A1</u> | November 25, 2004 |          | 000   | C12P021/04  |

DESIGNATED-STATES: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

## APPLICATION-DATA:

| PUB-NO          | APPL-DATE        | APPL-NO        | DESCRIPTOR |
|-----------------|------------------|----------------|------------|
| US20040253673A1 | March 16, 1995   | 1995US-0405496 | CIP of     |
| US20040253673A1 | August 28, 1996  | 1996US-0704159 | Cont of    |
| US20040253673A1 | October 15, 2002 | 2002US-0271012 | Div ex     |
| US20040253673A1 | December 5, 2003 | 2003US-0728696 |            |
| US20040253673A1 |                  | US 5919665     | CIP of     |
| WO 9808540A1    | August 28, 1997  | 1997WO-US15394 |            |

|                 |                  |                |          |
|-----------------|------------------|----------------|----------|
| AU 9742450A     | August 28, 1997  | 1997AU-0042450 |          |
| AU 9742450A     |                  | WO 9808540     | Based on |
| EP 1105153A1    | August 28, 1997  | 1997EP-0940746 |          |
| EP 1105153A1    | August 28, 1997  | 1997WO-US15394 |          |
| EP 1105153A1    |                  | WO 9808540     | Based on |
| US20030215468A1 | March 16, 1995   | 1995US-0405496 | CIP of   |
| US20030215468A1 | August 28, 1996  | 1996US-0704159 | Cont of  |
| US20030215468A1 | January 30, 2003 | 2003US-0354774 |          |
| US20030215468A1 |                  | US 5919665     | CIP of   |
| US20030219457A1 | March 16, 1995   | 1995US-0405496 | CIP of   |
| US20030219457A1 | August 28, 1996  | 1996US-0704159 | Cont of  |
| US20030219457A1 | October 15, 2002 | 2002US-0271012 |          |
| US20030219457A1 |                  | US 5919665     | CIP of   |
| US20040115215A1 | March 16, 1995   | 1995US-0405496 | CIP of   |
| US20040115215A1 | August 28, 1996  | 1996US-0704159 | Cont of  |
| US20040115215A1 | October 15, 2002 | 2002US-0271012 | Div ex   |
| US20040115215A1 | December 5, 2003 | 2003US-0729122 |          |
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| US20040142455A1 | March 16, 1995   | 1995US-0405496 | CIP of   |
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| US20040142455A1 | October 15, 2002 | 2002US-0271012 | Div ex   |
| US20040142455A1 | December 5, 2003 | 2003US-0729039 |          |
| US20040142455A1 |                  | US 5919665     | CIP of   |
| US20040219637A1 | March 16, 1995   | 1995US-0405496 | CIP of   |
| US20040219637A1 | August 28, 1996  | 1996US-0704159 | Cont of  |
| US20040219637A1 | October 15, 2002 | 2002US-0271012 | Div ex   |
| US20040219637A1 | December 5, 2003 | 2003US-0729527 |          |
| US20040219637A1 |                  | US 5919665     | CIP of   |
| US20040235118A1 | March 16, 1995   | 1995US-0405496 | CIP of   |
| US20040235118A1 | August 28, 1996  | 1996US-0704159 | Cont of  |
| US20040235118A1 | January 30, 2003 | 2003US-0354774 | Div ex   |
| US20040235118A1 | December 4, 2003 | 2003US-0727898 |          |
| US20040235118A1 |                  | US 5919665     | CIP of   |

INT-CL (IPC): A61 K 38/08; A61 K 39/00; A61 K 39/02; A61 K 39/08; A61 K 39/12; A61 K 39/38; A61 K 39/395; C07 H 21/04; C07 K 14/33; C07 K 16/00; C07 K 16/12; C12 N 1/18; C12 N 1/21; C12 N 5/06; C12 N 15/00; C12 N 15/09; C12 N 15/63; C12 N 15/70; C12 N 15/74; C12 P 21/02; C12 P 21/04; C12 P 21/06; C12 P 21/08; C12 Q 1/68

RELATED-ACC-NO: 1994-217494;1994-271898 ;1994-341765 ;1996-230603

ABSTRACTED-PUB-NO: WO 9808540A

BASIC-ABSTRACT:

Host cell, containing a recombinant expression vector, which encodes a protein comprising at least a portion of a Clostridium botulinum type B or E toxin, is claimed. Also claimed are: (1) a host cell containing a recombinant expression vector, which encodes a fusion protein comprising a non-toxin protein sequence, preferably comprising a poly-histidine tract, and at least a portion, preferably comprising the receptor binding domain, of a C. botulinum type B or E toxin; and (2) a vaccine, preferably endotoxin free, comprising the fusion protein of (1), and preferably further comprising a fusion protein comprising a non-toxin protein sequence and at least a portion of C. botulinum type A toxin.

USE - An antigen comprising the fusion protein can be used to generate a novel antibody (Ab) directed against a C. botulinum toxin (claimed). The vaccine and the Ab can be used to treat humans and other animals at risk of intoxication with clostridial toxin, while the Ab or the protein can also be used for the detection of bacterial toxins.

ABSTRACTED-PUB-NO: WO 9808540A

EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/40

DERWENT-CLASS: B04 D16

CPI-CODES: B04-E08; B04-G01; B04-N0300E; B12-K04A4; B14-A01; B14-S11B; D05-H07; D05-H11; D05-H14A1; D05-H17C;

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*Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.*

### Entry information

Entry name **BXA1\_CLOBO**  
Primary accession number **P10845**  
Secondary accession numbers P01561 P18639  
Entered in Swiss-Prot in Release 11, July 1989  
Sequence was last modified in Release 26, July 1993  
Annotations were last modified in Release 46, February 2005

### Name and origin of the protein

Protein name **Botulinum neurotoxin type A [Precursor]**  
Synonyms **EC 3.4.24.69**  
**BoNT/A**  
**Bontoxilysin A**  
**BOTOX**

Contains **Botulinum neurotoxin A, light-chain**  
**Botulinum neurotoxin A, heavy-chain**

Gene name **Name: botA**

Synonyms: atx, bna

From **Clostridium botulinum [TaxID: 1491]**

Taxonomy **Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium.**

### References

- [1] NUCLEOTIDE SEQUENCE.  
**STRAIN=Type A / NCTC 2916;**  
**MEDLINE=90235864;PubMed=2185020 [NCBI, ExPASy, EBI, Israel, Japan]**  
**Thompson D.E., Brehm J.K., Oultram J.D., Swinfield T.-J., Shone C.C., Atkinson T., Melling J., Minton N.P.;**  
**"The complete amino acid sequence of the Clostridium botulinum type A neurotoxin, deduced by nucleotide sequence analysis of the encoding gene.";**  
**Eur. J. Biochem. 189:73-81(1990).**
- [2] NUCLEOTIDE SEQUENCE.

**STRAIN**=Type A / 62A;

**MEDLINE**=90264400;PubMed=2160960 [NCBI, ExPASy, EBI, Israel, Japan]

Binz B., Kuarzono H., Wille M., Frevent J., Wernars K., Niemann H.;

"The complete sequence of botulinum neurotoxin type A and comparison with other clostridial neurotoxins.";

J. Biol. Chem. 265:9153-9158(1990).

[3] **NUCLEOTIDE SEQUENCE OF 1-65.**

**STRAIN**=Type A / 62A;

**MEDLINE**=97016817;PubMed=8863443 [NCBI, ExPASy, EBI, Israel, Japan]

East A.K., Bhandari M., Stacey J.M., Campbell K.D., Collins M.D.;

"Organization and phylogenetic interrelationships of genes encoding components of the botulinum toxin complex in proteolytic *Clostridium botulinum* types A, B, and F: evidence of chimeric sequences in the gene encoding the nontoxic nonhemagglutinin component.";

Int. J. Syst. Bacteriol. 46:1105-1112(1996).

[4] **NUCLEOTIDE SEQUENCE OF 1-34.**

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**MEDLINE**=89350959;PubMed=2669749 [NCBI, ExPASy, EBI, Israel, Japan]

Betley M.J., Somers E., Dasgupta B.R.;

"Characterization of botulinum type A neurotoxin gene: delineation of the N-terminal encoding region.";

Biochem. Biophys. Res. Commun. 162:1388-1395(1989).

[5] **NUCLEOTIDE SEQUENCE OF 1-18.**

**STRAIN**=Type A / NIH;

DOI=10.1016/0014-5793(95)01241-5;MEDLINE=96096783;PubMed=8521962 [NCBI, ExPASy, EBI, Israel, Japan]

Fujita R., Fujinaga Y., Inoue K., Nakajima H., Kumon H., Oguma K.;

"Molecular characterization of two forms of nontoxic-nonhemagglutinin components of *Clostridium botulinum* type A progenitor toxins.";

FEBS Lett. 376:41-44(1995).

[6] **PROTEIN SEQUENCE OF 1-16.**

**MEDLINE**=84178501;PubMed=6370252 [NCBI, ExPASy, EBI, Israel, Japan]

Schmidt J.J., Sartymoorthy V., Dasgupta B.R.;

"Partial amino acid sequence of the heavy and light chains of botulinum neurotoxin type A.";

Biochem. Biophys. Res. Commun. 119:900-904(1984).

[7] **PROTEIN SEQUENCE OF 1-46.**

Dasgupta B.R., Foley J., Niece R.;

"Partial sequence of the light chain of botulinum neurotoxin type A.";

Biochemistry 26:4162-4162(1987).

[8] **PROTEIN SEQUENCE OF 1-5 AND 444-456.**

DOI=10.1016/0300-9084(90)90048-L;MEDLINE=91120847;PubMed=2126206 [NCBI, ExPASy, EBI, Israel, Japan]

Dasgupta B.R., Dekleva M.L.;

"Botulinum neurotoxin type A: sequence of amino acids at the N-terminus and around the nicking site.";

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[9] **PROTEIN SEQUENCE OF 448-464 AND 872-895.**

**MEDLINE**=89024662;PubMed=3178218 [NCBI, ExPASy, EBI, Israel, Japan]

Sathymoorthy V., Dasgupta B.R., Foley J., Niece R.L.;

"Botulinum neurotoxin type A: cleavage of the heavy chain into two halves and their partial sequences.";

Arch. Biochem. Biophys. 266:142-151(1988).

[10] PROTEIN SEQUENCE OF 448-482.

MEDLINE=85285016;PubMed=3896784 [NCBI, ExPASy, EBI, Israel, Japan]

Shone C.C., Hambleton P., Melling J.;

"Inactivation of Clostridium botulinum type A neurotoxin by trypsin and purification of two tryptic fragments. Proteolytic action near the COOH-terminus of the heavy subunit destroys toxin-binding activity.";

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[11] PROTEIN SEQUENCE OF 866-879 AND 1147-1218.

PubMed=8397793 [NCBI, ExPASy, EBI, Israel, Japan]

Gimenez J.A., DasGupta B.R.;

"Botulinum type A neurotoxin digested with pepsin yields 132, 97, 72, 45, 42, and 18 kD fragments.";

J. Protein Chem. 12:351-363(1993).

[12] IDENTIFICATION OF SUBSTRATE.

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Schiavo G., Santtuci A., Dasgupta B.R., Mehta P.P., Jontes J., Benfenati F., Wilson M.C., Montecucco C.;

"Botulinum neurotoxins serotypes A and E cleave SNAP-25 at distinct COOH-terminal peptide bonds.";

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[13] IDENTIFICATION OF SUBSTRATE.

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Binz T., Blasi J., Yamasaki S., Baumeister A., Link E., Suedhof T.C., Jahn R., Niemann H.;

"Proteolysis of SNAP-25 by types E and A botulinal neurotoxins.";

J. Biol. Chem. 269:1617-1620(1994).

[14] MUTAGENESIS OF GLU-261; PHE-265 AND TYR-365.

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Rigoni M., Caccin P., Johnson E.A., Montecucco C., Rossetto O.;

"Site-directed mutagenesis identifies active-site residues of the light chain of botulinum neurotoxin type a.";

Biochem. Biophys. Res. Commun. 288:1231-1237(2001).

[15] X-RAY CRYSTALLOGRAPHY (3.3 ANGSTROMS).

MEDLINE=98455071;PubMed=9783750 [NCBI, ExPASy, EBI, Israel, Japan]

Lacy D.B., Tepp W., Cohen A.C., Dasgupta B.R., Stevens R.C.;

"Crystal structure of botulinum neurotoxin type A and implications for toxicity.";

Nat. Struct. Biol. 5:898-902(1998).

**Comments**

- **FUNCTION:** Inhibits acetylcholine release. The botulinum toxin binds with high affinity to peripheral neuronal presynaptic membrane, is then internalized by receptor-mediated endocytosis. The C-terminus of the heavy chain (H) is responsible for the adherence of the toxin to the cell surface while the N-terminus mediates transport of the light chain from the endocytic vesicle to the cytosol. After translocation, the light chain (L) hydrolyzes the 197-Gln-|-Arg-198 bond in SNAP-25, thereby blocking neurotransmitter release. Inhibition of acetylcholine release results in flaccid paralysis, with frequent heart or respiratory failure.
- **CATALYTIC ACTIVITY:** Limited hydrolysis of proteins of the neuroexocytosis apparatus, synaptobrevins, SNAP25 or syntaxin. No detected action on small molecule substrates.



- **COFACTOR**: Binds 1 zinc ion per subunit.
- **SUBUNIT**: Disulfide-linked heterodimer of a light chain (L) and a heavy chain (H).
- **SUBCELLULAR LOCATION**: Secreted.
- **PHARMACEUTICAL**: Available under the name BOTOX (Allergan) for the treatment of strabismus and blepharospasm associated with dystonia and cervical dystonia. Also used for the treatment of hemifacial spasm and a number of other neurological disorders characterized by abnormal muscle contraction.
- **MISCELLANEOUS**: There are seven antigenically distinct forms of botulinum neurotoxin: Types A, B, C1, D, E, F, and G.
- **SIMILARITY**: Belongs to the peptidase M27 family [view classification].
- **DATABASE**: NAME=BOTOX product information Web site; WWW="http://www.botox.com/site/".
- **DATABASE**: NAME=Protein Spotlight; NOTE=Issue 19 of February 2002; WWW="http://www.expasy.org/spotlight/back\_issues/sptlt019.shtml".

### Copyright

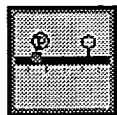
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### Cross-references

|              |   |
|--------------|---|
| EMBL         | X52066; CAA36289.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]<br>M30196; AAA23262.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]<br>X92973; CAA63551.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]<br>D67030; BAA11051.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]<br>M27892; AAA23269.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] |
| PIR          | A35294; BTCLAB.   |
| PDB          | 3BTA; X-ray; A=1-1295.[ExPASy / RCSB / EBI]   |
| MEROPS       | M27.002; -.<br>IPR008985; ConA_like_lectin.<br>IPR011065; Kunitz_like.  |
| InterPro     | IPR006025; Pept_M_Zn_BS.<br>IPR000395; Peptidase_M27.<br>Graphical view of domain structure.  |
| Pfam         | PF01742; Peptidase_M27; 1.<br>Pfam graphical view of domain structure.  |
| PRINTS       | PR00760; BONTOLYLIN.  |
| ProDom       | PD001963; Botulinum; 1.<br>[Domain structure / List of seq. sharing at least 1 domain]  |
| PROSITE      | PS00142; ZINC_PROTEASE; 1.  |
| HOBACGEN     | [Family / Alignment / Tree]   |
| BLOCKS       | P10845.   |
| ProtoNet     | P10845.   |
| ProtoMap     | P10845.   |
| PRESAGE      | P10845.   |
| DIP          | P10845.   |
| ModBase      | P10845.   |
| SMR          | P10845; 858342F754862579.   |
| SWISS-2DPAGE | Get region on 2D PAGE.  |
| UniRef       | View cluster of proteins with at least 50% / 90% identity.  |

**3D-structure; Direct protein sequencing; Hydrolase; Metalloprotease; Neurotoxin; Pharmaceutical; Transmembrane; Zinc.**

### Features



Feature table viewer



Feature aligner

| Key      | From | To   | Length | Description                                   |
|----------|------|------|--------|---|
| INIT_MET | 0    | 0    |        |   |
| CHAIN    | 1    | 447  | 447    | Botulinum neurotoxin A light-chain.           |
| CHAIN    | 448  | 1295 | 848    | Botulinum neurotoxin A heavy-chain.           |
| METAL    | 222  | 222  |        | Zinc (catalytic).                             |
| ACT_SITE | 223  | 223  |        |   |
| METAL    | 226  | 226  |        | Zinc (catalytic).                             |
| METAL    | 261  | 261  |        | Zinc (catalytic).                             |
| DISULFID | 429  | 453  |        | Interchain.                                   |
| DISULFID | 1234 | 1279 |        |   |
| TRANSMEM | 626  | 646  | 21     | Potential.                                    |
| TRANSMEM | 655  | 675  | 21     | Potential.                                    |
| VARIANT  | 26   | 26   | 1      | V -> A.                                       |
| MUTAGEN  | 261  | 261  |        | E->A: Drastic decrease in enzymatic activity. |
| MUTAGEN  | 265  | 265  |        | F->A: Decreases enzymatic activity.           |
| MUTAGEN  | 365  | 365  |        | Y->A: Decreases enzymatic activity.           |
| CONFLICT | 1    | 1    |        | P -> Q (in Ref. 1).                           |
| CONFLICT | 479  | 479  |        | E -> P (in Ref. 9).                           |
| CONFLICT | 875  | 875  |        | T -> L (in Ref. 8).                           |
| CONFLICT | 891  | 891  |        | S -> K (in Ref. 8).                           |
| CONFLICT | 1217 | 1217 |        | S -> Y (in Ref. 11).                          |
| TURN     | 9    | 10   | 2      |   |
| STRAND   | 18   | 22   | 5      |   |
| STRAND   | 25   | 25   | 1      |   |
| STRAND   | 32   | 38   | 7      |   |
| TURN     | 39   | 40   | 2      |   |
| STRAND   | 41   | 47   | 7      |   |
| HELIX    | 53   | 55   | 3      |   |
| TURN     | 74   | 77   | 4      |   |
| HELIX    | 80   | 98   | 19     |   |
| TURN     | 99   | 99   | 1      |   |
| HELIX    | 101  | 112  | 12     |   |
| TURN     | 119  | 120  | 2      |   |
| TURN     | 123  | 124  | 2      |   |
| HELIX    | 130  | 132  | 3      |   |
| STRAND   | 133  | 137  | 5      |   |
| TURN     | 139  | 140  | 2      |   |
| STRAND   | 143  | 147  | 5      |   |
| STRAND   | 150  | 154  | 5      |   |
| TURN     | 159  | 160  | 2      |   |
| STRAND   | 163  | 165  | 3      |   |
| STRAND   | 167  | 167  | 1      |   |

|        |     |     |    |
|--------|-----|-----|----|
| TURN   | 174 | 176 | 3  |
| STRAND | 183 | 186 | 4  |
| STRAND | 191 | 192 | 2  |
| STRAND | 194 | 195 | 2  |
| HELIX  | 200 | 202 | 3  |
| TURN   | 203 | 203 | 1  |
| TURN   | 205 | 206 | 2  |
| STRAND | 212 | 213 | 2  |
| HELIX  | 216 | 231 | 16 |
| TURN   | 232 | 233 | 2  |
| TURN   | 238 | 239 | 2  |
| STRAND | 241 | 241 | 1  |
| STRAND | 244 | 244 | 1  |
| STRAND | 251 | 251 | 1  |
| STRAND | 258 | 258 | 1  |
| HELIX  | 259 | 265 | 7  |
| TURN   | 267 | 268 | 2  |
| HELIX  | 269 | 272 | 4  |
| HELIX  | 275 | 297 | 23 |
| TURN   | 298 | 298 | 1  |
| STRAND | 305 | 305 | 1  |
| HELIX  | 309 | 320 | 12 |
| TURN   | 321 | 321 | 1  |
| STRAND | 323 | 324 | 2  |
| STRAND | 330 | 331 | 2  |
| HELIX  | 334 | 346 | 13 |
| TURN   | 347 | 347 | 1  |
| HELIX  | 350 | 356 | 7  |
| TURN   | 357 | 358 | 2  |
| TURN   | 365 | 366 | 2  |
| STRAND | 373 | 374 | 2  |
| TURN   | 380 | 382 | 3  |
| STRAND | 384 | 384 | 1  |
| TURN   | 385 | 387 | 3  |
| STRAND | 388 | 388 | 1  |
| TURN   | 389 | 389 | 1  |
| HELIX  | 401 | 403 | 3  |
| STRAND | 404 | 404 | 1  |
| TURN   | 405 | 408 | 4  |
| HELIX  | 409 | 411 | 3  |
| STRAND | 413 | 414 | 2  |
| TURN   | 420 | 422 | 3  |
| STRAND | 425 | 430 | 6  |
| STRAND | 453 | 457 | 5  |
| HELIX  | 458 | 460 | 3  |
| STRAND | 462 | 462 | 1  |
| STRAND | 465 | 465 | 1  |

|        |     |     |    |
|--------|-----|-----|----|
| TURN   | 467 | 469 | 3  |
| TURN   | 474 | 475 | 2  |
| STRAND | 478 | 480 | 3  |
| HELIX  | 495 | 503 | 9  |
| TURN   | 504 | 504 | 1  |
| STRAND | 516 | 516 | 1  |
| STRAND | 524 | 524 | 1  |
| STRAND | 527 | 527 | 1  |
| STRAND | 541 | 544 | 4  |
| HELIX  | 549 | 554 | 6  |
| TURN   | 555 | 556 | 2  |
| HELIX  | 572 | 575 | 4  |
| TURN   | 576 | 576 | 1  |
| TURN   | 578 | 579 | 2  |
| HELIX  | 587 | 593 | 7  |
| TURN   | 599 | 600 | 2  |
| HELIX  | 603 | 616 | 14 |
| TURN   | 617 | 618 | 2  |
| STRAND | 621 | 621 | 1  |
| TURN   | 624 | 625 | 2  |
| TURN   | 627 | 628 | 2  |
| STRAND | 632 | 632 | 1  |
| HELIX  | 634 | 636 | 3  |
| TURN   | 637 | 643 | 7  |
| HELIX  | 651 | 658 | 8  |
| HELIX  | 660 | 663 | 4  |
| STRAND | 678 | 680 | 3  |
| TURN   | 684 | 685 | 2  |
| HELIX  | 687 | 719 | 33 |
| TURN   | 720 | 720 | 1  |
| HELIX  | 721 | 741 | 21 |
| TURN   | 742 | 744 | 3  |
| HELIX  | 745 | 750 | 6  |
| TURN   | 751 | 752 | 2  |
| TURN   | 757 | 758 | 2  |
| HELIX  | 765 | 798 | 34 |
| TURN   | 799 | 799 | 1  |
| HELIX  | 800 | 823 | 24 |
| TURN   | 824 | 828 | 5  |
| HELIX  | 830 | 832 | 3  |
| TURN   | 833 | 834 | 2  |
| HELIX  | 835 | 843 | 9  |
| TURN   | 844 | 845 | 2  |
| HELIX  | 852 | 854 | 3  |
| HELIX  | 859 | 870 | 12 |
| HELIX  | 872 | 875 | 4  |
| STRAND | 878 | 883 | 6  |
| TURN   | 884 | 885 | 2  |

|        |      |      |    |
|--------|------|------|----|
| STRAND | 886  | 889  | 4  |
| TURN   | 890  | 891  | 2  |
| STRAND | 894  | 899  | 6  |
| STRAND | 904  | 905  | 2  |
| TURN   | 910  | 911  | 2  |
| STRAND | 912  | 916  | 5  |
| TURN   | 919  | 920  | 2  |
| STRAND | 923  | 927  | 5  |
| TURN   | 930  | 931  | 2  |
| HELIX  | 934  | 937  | 4  |
| STRAND | 940  | 947  | 8  |
| TURN   | 955  | 958  | 4  |
| STRAND | 960  | 965  | 6  |
| STRAND | 974  | 978  | 5  |
| STRAND | 981  | 987  | 7  |
| TURN   | 989  | 990  | 2  |
| STRAND | 993  | 999  | 7  |
| TURN   | 1010 | 1011 | 2  |
| STRAND | 1013 | 1020 | 8  |
| TURN   | 1022 | 1023 | 2  |
| STRAND | 1025 | 1030 | 6  |
| TURN   | 1031 | 1032 | 2  |
| STRAND | 1033 | 1039 | 7  |
| TURN   | 1041 | 1042 | 2  |
| STRAND | 1051 | 1057 | 7  |
| TURN   | 1062 | 1063 | 2  |
| STRAND | 1065 | 1074 | 10 |
| HELIX  | 1080 | 1089 | 10 |
| TURN   | 1090 | 1091 | 2  |
| TURN   | 1093 | 1094 | 2  |
| STRAND | 1095 | 1095 | 1  |
| STRAND | 1097 | 1097 | 1  |
| TURN   | 1099 | 1100 | 2  |
| STRAND | 1103 | 1103 | 1  |
| STRAND | 1105 | 1105 | 1  |
| STRAND | 1110 | 1112 | 3  |
| TURN   | 1118 | 1119 | 2  |
| STRAND | 1121 | 1124 | 4  |
| TURN   | 1129 | 1130 | 2  |
| STRAND | 1133 | 1136 | 4  |
| STRAND | 1141 | 1141 | 1  |
| STRAND | 1151 | 1151 | 1  |
| STRAND | 1158 | 1162 | 5  |
| STRAND | 1172 | 1172 | 1  |
| STRAND | 1174 | 1174 | 1  |
| TURN   | 1175 | 1176 | 2  |
| STRAND | 1178 | 1185 | 8  |
| TURN   | 1186 | 1187 | 2  |

|        |      |      |   |
|--------|------|------|---|
| STRAND | 1188 | 1194 | 7 |
| TURN   | 1196 | 1197 | 2 |
| STRAND | 1206 | 1208 | 3 |
| TURN   | 1210 | 1212 | 3 |
| TURN   | 1214 | 1215 | 2 |
| STRAND | 1217 | 1217 | 1 |
| STRAND | 1220 | 1222 | 3 |
| STRAND | 1225 | 1225 | 1 |
| TURN   | 1227 | 1228 | 2 |
| STRAND | 1231 | 1231 | 1 |
| STRAND | 1234 | 1234 | 1 |
| STRAND | 1236 | 1238 | 3 |
| TURN   | 1241 | 1242 | 2 |
| STRAND | 1247 | 1252 | 6 |
| STRAND | 1259 | 1263 | 5 |
| HELIX  | 1264 | 1269 | 6 |
| TURN   | 1270 | 1271 | 2 |
| TURN   | 1278 | 1279 | 2 |
| STRAND | 1280 | 1280 | 1 |
| STRAND | 1283 | 1284 | 2 |
| TURN   | 1288 | 1289 | 2 |

**Sequence information**

Length: **1295 AA** [This is the length of the unprocessed precursor]

Molecular weight: **149323 Da** [This is the MW of the unprocessed precursor]

CRC64: **858342F754862579** [This is a checksum on the sequence]

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|------------|------------|-------------|-------------|------------|------------|
| <u>10</u>  | <u>20</u>  | <u>30</u>   | <u>40</u>   | <u>50</u>  | <u>60</u>  |
| PFVNKQFNYK | DPVNGVDIAY | IKIPNVGQMQ  | PVKAFKIHNK  | IWVIPERDTF | TNPEEGDLNP |
| <u>70</u>  | <u>80</u>  | <u>90</u>   | <u>100</u>  | <u>110</u> | <u>120</u> |
| PPEAKQVPVS | YYDSTYLSTD | NEKDNYLKGV  | TKLFERIYST  | DLGRMLLSI  | VRGIPFWGGS |
| <u>130</u> | <u>140</u> | <u>150</u>  | <u>160</u>  | <u>170</u> | <u>180</u> |
| TIDTELKVID | TNCINVIQPD | GSYRSEELNL  | VIIGPSADII  | QFECKSFGHE | VLNLTRNGYG |
| <u>190</u> | <u>200</u> | <u>210</u>  | <u>220</u>  | <u>230</u> | <u>240</u> |
| STQYIRFSPD | FTFGFEESLE | VDTNPLLGGAG | KFATDPAVTL  | AHELIHAGHR | LYGIAINPNR |
| <u>250</u> | <u>260</u> | <u>270</u>  | <u>280</u>  | <u>290</u> | <u>300</u> |
| VFKVNTNAYY | EMSGLEVSFE | ELRTFGGHDA  | KFIDSLQENE  | FRLYYYNKFK | DIASLTNKA  |
| <u>310</u> | <u>320</u> | <u>330</u>  | <u>340</u>  | <u>350</u> | <u>360</u> |
| SIVGTTASLQ | YMKNVFKEY  | LLSEDTSKGF  | SVDKLFKFDKL | YKMLTEIYTE | DNFVKFFKVL |
| <u>370</u> | <u>380</u> | <u>390</u>  | <u>400</u>  | <u>410</u> | <u>420</u> |
| NRKTYLNFDK | AVFKINIVPK | VNYTIYDGFN  | LRNTNLAANF  | NGQNTNINNM | NFTKLKNFTG |
| <u>430</u> | <u>440</u> | <u>450</u>  | <u>460</u>  | <u>470</u> | <u>480</u> |
| LFEFYKLLCV | RGIITSKTKS | LDKGYNKALN  | DLCIKVNNWD  | LFFSPSEDNF | TNDLNKGEEI |
| <u>490</u> | <u>500</u> | <u>510</u>  | <u>520</u>  | <u>530</u> | <u>540</u> |
| TSDTNIEAAE | ENISLDLIQQ | YYLTFNFDNE  | PENISIENLS  | SDIIGQLELM | PNIERFPNGK |
| <u>550</u> | <u>560</u> | <u>570</u>  | <u>580</u>  | <u>590</u> | <u>600</u> |

```

KYELDKYTMF HYLRAQEFEH GKSRIALTNS VNEALLNPSR VYTFSSDYV KKVNKATEAA
      610      620      630      640      650      660
MFLGWVEQLV YDFTDETSEV STTDKIADIT IIIPYIGPAL NIGNMLYKDD FVGALIFSGA
      670      680      690      700      710      720
VILLEFIPEI AIPVLGTFAL VSYIANKVLV VQTIDNALS RNEKWDEVYK YIVTNWLAKV
      730      740      750      760      770      780
NTQIDLIRKK MKEALENQAE ATKAIINYQY NQYTEEEKNN INFNIDDLSS KLNESINKAM
      790      800      810      820      830      840
ININKFLNQC SVSYLMNSMI PYGVKRLEDF DASLKDALLK YIIDNRGTLI GQVDRCLKDKV
      850      860      870      880      890      900
NNTLSTDIPF QLSKYVDNQR LLSTFTEYIK NIINTSILNL RYESNHLIDL SRYASKINIG
      910      920      930      940      950      960
SKVNFDPIDK NQIQLFNLES SKIEVILKNA IVYNSMYENF STSFWIRIPK YFNSISLNNE
      970      980      990      1000     1010     1020
YTIINCMENN SGWKVSLNYG EIIWTLQDTQ EIKQRVVFKY SQMINISDYI NRWIFVTITN
      1030     1040     1050     1060     1070     1080
NRLNNSKIYI NGRLIDQKPI SNLGNIHASN NIMFKLDGCR DTHRYIWIKY FNLFDKELNE
      1090     1100     1110     1120     1130     1140
KEIKDLYDNQ SNSGILKDFW GDYLQYDKPY YMLNLYDPNK YVDVNVVGIR GYMYLKGRG
      1150     1160     1170     1180     1190     1200
SVMTTNIYLN SSLYRGTKFI IKKYASGNKD NIVRNNDRVY INVVVKNKEY RLATNASQAG
      1210     1220     1230     1240     1250     1260
VEKILSALEI PDVGNLSQVV VMKSKNDQGI TNKCKMNLQD NNGNDIGFIG FHQFNNTIAKL
      1270     1280     1290
VASNWNRYQI ERSRSLGCS WEFIPVDDGW GERPL

```

P10845 in FASTA  
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BLAST

BLAST submission on  
ExPASy/SIB  
or at NCBI (USA)



Sequence analysis tools: ProtParam, ProtScale,  
Compute pI/Mw, PeptideMass, PeptideCutter,  
Dotlet (Java)




ScanProsite, MotifScan



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|--|--------------------------|-------------------------------|----------------------------|----------------------------|

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## View of

## TrEMBL:

## Q84GJ4

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[\[Features\]](#) [\[Sequence\]](#) [\[Tools\]](#)

*Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.*

### Entry information

|                                   |                        |
|-----------------------------------|------------------------|
| Entry name                        | <b>Q84GJ4_CLOBO</b>    |
| Primary accession number          | <b>Q84GJ4</b>          |
| Secondary accession numbers       | None                   |
| Entered in TrEMBL in              | Release 24, June 2003  |
| Sequence was last modified in     | Release 24, June 2003  |
| Annotations were last modified in | Release 26, March 2004 |

### Name and origin of the protein

|              |   |
|--------------|---|
| Protein name | <b>Neurotoxin type A light chain [Fragment]</b>                               |
| Synonyms     | None  |
| Gene name    | None  |
| From         | Clostridium botulinum [TaxID: 1491]   |
| Taxonomy     | Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium. |

### References

- [1] NUCLEOTIDE SEQUENCE.  
 Seong H.Y., Kim J.S., Lee M.H., Choi Y.M., Choi S.-Y.;  
 Submitted (OCT-2002) to the EMBL/GenBank/DDBJ databases.

### Comments

None

### Cross-references

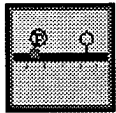
|      |  |
|------|--|
| EMBL | AY166872; AAO21363.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]  |
| HSSP | P10845; 3BTA. [HSSP ENTRY / PDB]   |
|      | GO:0008233; Molecular function: peptidase activity ( <i>inferred from electronic annotation</i> ).           |
|      | GO:0009405; Biological process: pathogenesis ( <i>inferred from electronic annotation</i> ).                 |
| GO   | GO:0006508; Biological process: proteolysis and peptidolysis ( <i>inferred from electronic annotation</i> ). |
|      | QuickGo<br>view.   |
|      | IPR011591; Botulinum.  |



InterPro IPR000395; Peptidase\_M27.  
 IPR006025; Pept\_M\_Zn\_BS.  
 Graphical view of domain structure.  
 Pfam PF01742; Peptidase\_M27; 1.  
 Pfam graphical view of domain structure.  
 PRINTS PR00760; BONTOXILYSIN.  
 ProDom PD001963; Botulinum; 1.  
 [Domain structure / List of seq. sharing at least 1 domain]  
 PROSITE PS00142; ZINC\_PROTEASE; UNKNOWN\_1.  
 HOBACGEN [Family / Alignment / Tree]  
 ProtoMap Q84GJ4.  
 PRESAGE Q84GJ4.  
 ModBase Q84GJ4.  
 SMR Q84GJ4; 89C98D162AC9FDBE.  
 SWISS-2DPAGE Get region on 2D PAGE.  
 UniRef View cluster of proteins with at least 50% / 90% identity.

**Keywords**

Neurotoxin; Toxin.

**Features**

Feature table viewer

| Key     | From | To  | Length | Description |
|---------|------|-----|--------|-------------|
| NON_TER | 448  | 448 |        |             |

**Sequence information**

Length: **448 AA** [This is the length of the partial sequence]  
 Molecular weight: **51325 Da** [This is the MW of the partial sequence]

CRC64: **89C98D162AC9FDBE** [This is a checksum on the sequence]

|            |            |            |            |            |            |
|------------|------------|------------|------------|------------|------------|
| <u>10</u>  | <u>20</u>  | <u>30</u>  | <u>40</u>  | <u>50</u>  | <u>60</u>  |
| MPFVNKQFNY | KDPVNGVDIA | YIKIPNAGQM | QVKAFKIHNK | IWVIPERDTF | TNPEEGDLNP |
| <u>70</u>  | <u>80</u>  | <u>90</u>  | <u>100</u> | <u>110</u> | <u>120</u> |
| PPEAKQVPVS | YYDSTYLSTD | NEKDNYLKGV | TKLFERIYST | DLGRMLLSI  | VRGIPFWGGS |
| <u>130</u> | <u>140</u> | <u>150</u> | <u>160</u> | <u>170</u> | <u>180</u> |
| TIDTELKVID | TNCINVIQPD | GSYRSEELNL | VIIGPSADII | QFECKSFGHE | VLNLTRNGYG |
| <u>190</u> | <u>200</u> | <u>210</u> | <u>220</u> | <u>230</u> | <u>240</u> |
| STQYIRFSPD | FTFGFEESLE | VDTNPLLGA  | KFATDPAVTL | AHELIHAGHR | LYGIAINPNR |
| <u>250</u> | <u>260</u> | <u>270</u> | <u>280</u> | <u>290</u> | <u>300</u> |
| VFKVNTNAYY | EMSGLEVSFE | ELRTFGGHDA | KFIDSLQENE | FRLYYYNKF  | DIASLTNKA  |
| <u>310</u> | <u>320</u> | <u>330</u> | <u>340</u> | <u>350</u> | <u>360</u> |
| SIVGTTASLQ | YMKNVFKEY  | LLSEDTSGKF | SVDKLKFDKL | YKMKTEIYTE | DDNFVKFFKV |
| <u>370</u> | <u>380</u> | <u>390</u> | <u>400</u> | <u>410</u> | <u>420</u> |
| LNRKTYLNF  | KAVFKINIVP | KVNYTIYDGF | NLRNTNLAAN | FNGQNTINN  | MNFTKLKNFT |

430 440  
GLFEFYKLLC VRGIITSKTK SLDEGYNK

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ExPASy/SIB  
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Compute pI/Mw, PeptideMass, PeptideCutter,  
Dotlet (Java)



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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/15394

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/184.1, 192.1, 247.1; 435/69.1, 69.7, 325, 320.1; 530/388.4, 389.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MEDLINE, BIOSIS, WPIDS, CAPLUS, APS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|-----------|---|-----------------------|
| Y         | THOMPSON et al. The Complete Amino Acid Sequence of the Clostridium botulinum Type A Neurotoxin, Deduced by Nucleotide Sequence Analysis of the Encoding Gene. Eur. J. Biochem. April 1990, Vol. 189, pages 73-81, see entire document. | 1-24                  |
| Y         | BINZ et al. The Complete Sequence of Botulinum Neurotoxin Type A and Comparison with Other Clostridial Neurotoxins. Journal of Biological Chemistry. June 1990, Vol. 265, No. 16, pages 9153-9158, see entire document.                 | 1-24                  |
| Y         | ROITT. Essential Immunology. Oxford: Blackwell Scientific Publications. 1988, especially pages 173-178.   | 1-24                  |

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

|  |  |
|--|--|
| * Special categories of cited documents:   | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| *A* document defining the general state of the art which is not considered to be of particular relevance   | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
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Date of the actual completion of the international search

10 OCTOBER 1997

Date of mailing of the international search report

23 DEC 1997

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

EVELYN RABIN

Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/15394

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|-----------|--|-----------------------|
| Y         | SIEGEL. Human Immune Response to Botulinum Pentavalent (ABCDE) Toxoid Determined by a Neutralization Test and by an Enzyme-Linked Immunosorbent Assay. Journal of Clinical Microbiology. November 1988, Vol. 26, pages 2351-2356, see entire document. | 1-24                  |
| Y         | FORD et al. Fusion Tails for the Recovery and Purification of Recombinant Proteins. Protein Expression Purification. 1991, Vol. 2, pages 95-107, see entire document.  | 1-24                  |
| Y         | LECLERC et al. Induction of Virus-Neutralizing Antibodies by Bacteria Expressing the C3 Poliovirus Epitope in the Periplasm. Journal of Immunology. April 1990, Vol. 144, pages 3174-3182, see entire document.  | 1-24                  |
| Y         | KLEID. Using Genetically Engineered Bacteria for Vaccine Production. Annals New York Acad. Sci. 1983, Vol. 483, pages 23-30, see entire document.  | 1-24                  |

Form PCT/ISA/210 (continuation of second sheet)(July 1992)\*

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US97/15394

A. CLASSIFICATION OF SUBJECT MATTER:  
IPC (6):

A61K 39/00, 39/38, 38/08; C12P 21/06, 21/04, 21/08; C12N 15/00, 15/09, 15/63, 15/70, 15/74; C07K 16/00

A. CLASSIFICATION OF SUBJECT MATTER:  
US CL :

424/184.1, 192.1, 247.1; 435/69.1, . 69.7, 325, 320.1; 530/388.4, 389.5